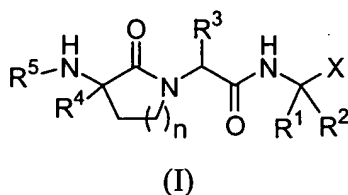


1. (Currently amended) A method for treating a cancer that is responsive to proteasome inhibition comprising administering to a mammal in need thereof, either alone or in combination with at least one other anticancer agent, a therapeutically effective amount of a compound of Formula I:



or a stereoisomer or pharmaceutically acceptable salt form thereof, wherein

the lactam ring of Formula (I) is substituted with 0-2 R^b;

X is selected from the group:

B(OH)₂, BY¹Y², and C(=O)C(=O)NHR^{1a};

Y¹ and Y² are independently selected from:

- a) -OH,
- b) -F,
- c) -NR¹⁸R¹⁹,
- d) C₁-C₈ alkoxy, or

when taken together, Y¹ and Y² form:

- e) a cyclic boron ester comprising from 2 to 20 carbon atoms, and, optionally, 1, 2, or 3 heteroatoms which can be N, S, or O;
- f) a cyclic boron amide comprising from 2 to 20 carbon atoms and, optionally, 1, 2, or 3 heteroatoms which can be N, S, or O; or
- g) a cyclic boron amide-ester comprising from 2 to 20 carbon atoms and, optionally, 1, 2, or 3 heteroatoms which can be N, S, or O;

R¹ is selected from the group:

C₁₋₁₀ alkyl substituted with 0-3 R^a;
C₂₋₁₀ alkenyl substituted with 0-3 R^a;
C₂₋₁₀ alkynyl substituted with 0-3 R^a; and
C₃₋₆ cycloalkyl substituted with 0-3 R^a;

R^{1a} is selected from the group:

C₁₋₁₀ alkyl substituted with 0-3 R^a;
C₂₋₁₀ alkenyl substituted with 0-3 R^a;
C₂₋₁₀ alkynyl substituted with 0-3 R^a; and
C₃₋₆ cycloalkyl substituted with 0-3 R^a;

R^a is selected at each occurrence from the group:

C₁₋₃ alkyl, C₃₋₆ cycloalkyl, Cl, F, Br, I, CF₃, OH, =O, C₁₋₆ alkoxy, SH, -S-C₁₋₆ alkyl;
phenyl substituted with 0-3 R^b;
naphthyl substituted with 0-3 R^b;
-O-(CH₂)_q-phenyl substituted with 0-3 R^b;
-O-(CH₂)_q-naphthyl substituted with 0-3 R^b; and
5-10 membered heteroaryl consisting of carbon atoms and 1-4 heteroatoms selected from the group:
O, S, and N, and substituted with 0-3 R^b;

R^b is selected at each occurrence from the group:

C₁₋₆ alkyl, Cl, F, Br, I, OH, C₁₋₆ alkoxy, -CN, -NO₂, C(O)OR⁷, NR^dR^d, CF₃, OCF₃, and C₃₋₆ cycloalkyl;

R² is H;

alternatively, R¹ and R² combine to form a C₃₋₅ cycloalkyl group;

R³ is selected from the group:

- C₁₋₆ alkyl substituted with 0-2 R^a;
- C₂₋₆ alkenyl substituted with 0-2 R^a;
- C₂₋₆ alkynyl substituted with 0-2 R^a;
- (CH₂)_q-C₃₋₆ cycloalkyl substituted with 0-2 R^a;
- (CH₂)_q-phenyl substituted with 0-2 R^a;
- (CH₂)_q-naphthyl substituted with 0-2 R^a; and
- (CH₂)_q-5-10 membered heteroaryl consisting of carbon atoms and 1-4 heteroatoms selected from the group:
O, S, and N, and substituted with 0-2 R^a;

R⁴ is selected from the group:

- H;
- C₁₋₆ alkyl substituted with 0-3 R^b;
- phenyl substituted with 0-3 R^b;
- benzyl substituted with 0-3 R^b; and
- phenethyl substituted with 0-3 R^b;

R⁵ is H or Q-R^{5a};

Q is 0, 1, 2, or 3 amino acids;

R^{5a} is selected from the group:

- S(O)R⁶, -S(O)₂R⁶, -C(O)R⁶, -C(O)OR⁸, -C(O)NHR⁶, C₁₋₃ alkyl-R^{6a}, C₂₋₆ alkenyl-R^{6a}, and C₂₋₆ alkynyl-R^{6a};

R⁶ is selected from the group:

- C₁₋₆ alkyl substituted with 0-3 R^c;

phenyl substituted with 0-3 R^c;
naphthyl substituted with 0-3 R^c;
benzyl substituted with 0-3 R^c; and
5-10 membered heteroaryl consisting of carbon atoms and 1-4 heteroatoms
selected from the group:
O, S, and N, substituted with 0-3 R^c;

R^{6a} is selected from the group:

phenyl substituted with 0-3 R^c;
naphthyl substituted with 0-3 R^c;
benzyl substituted with 0-3 R^c; and
5-10 membered heteroaryl consisting of carbon atoms and 1-4 heteroatoms
selected from the group:
O, S, and N, substituted with 0-3 R^c;

R^c is selected at each occurrence from the group:

C₁₋₄ alkyl, C₁₋₄ alkoxy, CF₃, OCF₃, Cl, F, Br, I, =O, OH, phenyl, C(O)OR⁷,
NR^dR^d, -CN, and NO₂;

R^d is selected at each occurrence from the group:

H and CH₃;

R⁷ is selected at each occurrence from the group:

H and C₁₋₆ alkyl;

R⁸ is selected from the group:

C₁₋₆ alkyl, benzyl, and C₃₋₆ cycloalkyl-methyl;

R¹⁸ and R¹⁹ at each occurrence are independently selected from H, C₁₋₄ alkyl, aryl(C₁₋₄ alkyl)-, and C₃₋₇ cycloalkyl;

n is selected from the group:

1, 2, and 3; and

q is selected the group:

0, 1, and 2.

2. (Original) The method according to claim 1 wherein:

Y¹ and Y² are independently selected from:

a) -OH,

b) C₁-C₈ alkoxy, or

when taken together, Y¹ and Y² form:

c) a cyclic boron ester comprising from 2 to 20 carbon atoms;

R¹ is selected from the group:

C₁₋₆ alkyl substituted with 0-3 halogen; and

C₂₋₆ alkenyl substituted with 0-3 halogen;

R^a is selected at each occurrence from the group:

C₁₋₃ alkyl, C₃₋₆ cycloalkyl, Cl, F, Br, I, CF₃, OH, =O, C₁₋₆ alkoxy, SH, -S-C₁₋₆ alkyl;

phenyl substituted with 0-3 R^b;

naphthyl substituted with 0-3 R^b;

-O-(CH₂)_q-phenyl substituted with 0-3 R^b;

-O-(CH₂)_q-naphthyl substituted with 0-3 R^b; and

5-10 membered heteroaryl consisting of carbon atoms and 1-4 heteroatoms selected from the group:

O, S, and N, and substituted with 0-3 R^b;

R^b is selected at each occurrence from the group:

C₁₋₆ alkyl, Cl, F, Br, I, OH, C₁₋₆ alkoxy, -CN, -NO₂, C(O)OR⁷, NR^dR^d, CF₃,
OCF₃, and C₃₋₆ cycloalkyl;

R² is H;

R³ is selected from the group:

C₁₋₆ alkyl substituted with 0-2 R^a;

C₂₋₆ alkenyl substituted with 0-2 R^a;

C₂₋₆ alkynyl substituted with 0-2 R^a;

-(CH₂)_q-C₃₋₆ cycloalkyl substituted with 0-2 R^a;

-(CH₂)_q-phenyl substituted with 0-2 R^a;

-(CH₂)_q-naphthyl substituted with 0-2 R^a; and

-(CH₂)_q-5-10 membered heteroaryl consisting of carbon atoms and 1-4

heteroatoms selected from the group:

O, S, and N, and substituted with 0-2 R^a;

R⁴ is selected from the group:

H;

C₁₋₆ alkyl substituted with 0-3 R^b;

phenyl substituted with 0-3 R^b;

benzyl substituted with 0-3 R^b; and

phenethyl substituted with 0-3 R^b;

R⁵ is H or Q-R^{5a};

Q is 0, 1, 2, or 3 amino acids;

R^{5a} is selected from the group:

-S(O)R⁶, -S(O)₂R⁶, -C(O)R⁶, -C(O)OR⁸, -C(O)NHR⁶, C₁₋₃ alkyl-R^{6a}, C₂₋₆ alkenyl-R^{6a}, and C₂₋₆ alkynyl-R^{6a};

R⁶ is selected from the group:

C₁₋₆ alkyl substituted with 0-3 R^c;
phenyl substituted with 0-3 R^c;
naphthyl substituted with 0-3 R^c;
benzyl substituted with 0-3 R^c; and
5-10 membered heteroaryl consisting of carbon atoms and 1-4 heteroatoms
selected from the group:
O, S, and N, substituted with 0-3 R^c;

R^{6a} is selected from the group:

phenyl substituted with 0-3 R^c;
naphthyl substituted with 0-3 R^c;
benzyl substituted with 0-3 R^c; and
5-10 membered heteroaryl consisting of carbon atoms and 1-4 heteroatoms
selected from the group:
O, S, and N, substituted with 0-3 R^c;

R^c is selected at each occurrence from the group:

C₁₋₄ alkyl, C₁₋₄ alkoxy, CF₃, OCF₃, Cl, F, Br, I, =O, OH, phenyl, C(O)OR⁷,
NR^dR^d, -CN, and NO₂;

R^d is selected at each occurrence from the group:

H and CH₃;

R⁷ is selected at each occurrence from the group:

H and C₁₋₆ alkyl;

R⁸ is selected from the group:

C₁₋₆ alkyl, benzyl, and C₃₋₆ cycloalkyl-methyl;

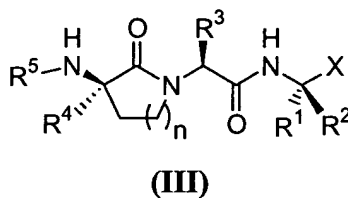
n is selected from the group:

1, 2, and 3; and

q is selected from the group:

0, 1, and 2.

3. (Original) A method for treating cancer comprising administering to a mammal in need thereof, either alone or in combination with at least one other anticancer agent, compound having Formula (III):



or a stereoisomer or pharmaceutically acceptable salt form thereof, wherein:

X is a boronic acid or a boron ester of formula BY¹Y²;

Y¹ and Y² are independently selected from:

a) C₁-C₆ alkoxy, or

when taken together, Y¹ and Y² form:

b) a cyclic boron ester comprising from 2 to 16 carbon atoms;

R¹ is selected from the group:

ethyl, n-propyl, i-propyl, n-butyl, allyl, 2,2,2-trifluoroethyl, 2,2-difluoroethyl, 3,3,3-trifluoropropyl, 4,4,4-trifluorobutyl, and 3-butenyl;

R^a is selected at each occurrence from the group:

C₁₋₃ alkyl, C₃₋₆ cycloalkyl, Cl, F, Br, I, CF₃, OH, =O, C₁₋₆ alkoxy, SH,

-S-C₁₋₆ alkyl;

phenyl substituted with 0-3 R^b;

naphthyl substituted with 0-3 R^b;

-O-(CH₂)_q-phenyl substituted with 0-3 R^b;

-O-(CH₂)_q-naphthyl substituted with 0-3 R^b; and

5-10 membered heteroaryl consisting of carbon atoms and 1-4 heteroatoms

selected from the group:

O, S, and N, and substituted with 0-3 R^b;

R^b is selected at each occurrence from the group:

C₁₋₆ alkyl, Cl, F, Br, I, OH, C₁₋₆ alkoxy, -CN, -NO₂, C(O)OR⁷, NR^dR^d, CF₃,

OCF₃, and C₃₋₆ cycloalkyl;

R² is H;

R³ is selected from the group:

C₁₋₆ alkyl substituted with 0-2 R^a;

C₂₋₆ alkenyl substituted with 0-2 R^a;

C₂₋₆ alkynyl substituted with 0-2 R^a;

-(CH₂)_q-C₃₋₆ cycloalkyl substituted with 0-2 R^a;

-(CH₂)_q-phenyl substituted with 0-2 R^a;

-(CH₂)_q-naphthyl substituted with 0-2 R^a;

-(CH₂)_q-5-10 membered heteroaryl consisting of carbon atoms and 1-4

heteroatoms selected from the group:

O, S, and N, and substituted with 0-2 R^a;

R⁴ is selected from the group:

H, methyl, ethyl, n-propyl, i-propyl, n-butyl, i-butyl, sec-butyl, t-butyl;
phenyl substituted with 0-3 R^b;
benzyl substituted with 0-3 R^b; and
phenethyl substituted with 0-3 R^b;

R⁵ is H or Q-R^{5a};

Q is 0, 1, or 2 amino acids;

R^{5a} is selected from the group:

-S(O)R⁶, -S(O)₂R⁶, -C(O)R⁶, -C(O)OR⁸, -C(O)NHR⁶, C₁₋₃ alkyl-R^{6a}, C₂₋₆
alkenyl-R^{6a}, and C₂₋₆ alkynyl-R^{6a};

R⁶ is selected from the group:

C₁₋₆ alkyl substituted with 0-3 R^c;
phenyl substituted with 0-3 R^c;
naphthyl substituted with 0-3 R^c;
benzyl substituted with 0-3 R^c; and
5-10 membered heteroaryl consisting of carbon atoms and 1-4 heteroatoms
selected from the group: O, S, and N, substituted with 0-3 R^c;

R^{6a} is selected from the group:

phenyl substituted with 0-3 R^c;
naphthyl substituted with 0-3 R^c;
benzyl substituted with 0-3 R^c; and
5-10 membered heteroaryl consisting of carbon atoms and 1-4 heteroatoms
selected from the group: O, S, and N, substituted with 0-3 R^c;

R^c is selected at each occurrence from the group:

C₁₋₄ alkyl, C₁₋₄ alkoxy, CF₃, OCF₃, Cl, F, Br, I, =O, OH, phenyl, C(O)OR⁷,
NR^dR^d, -CN, and NO₂;

R^d is selected at each occurrence from the group:

H and CH₃;

R⁷ is selected at each occurrence from the group:

H and C₁₋₆ alkyl;

R⁸ is selected from the group:

C₁₋₆ alkyl, benzyl, and C₃₋₆ cycloalkyl-methyl;

n is 1 or 2; and

q is selected from the group:

0, 1, and 2.

4. (Original) The method of claim 3 wherein:

X is a boronic acid or boron ester, wherein the ester is a diol selected from the group:

pinanediol, pinacol, 1,2-ethanediol, 1,3-propanediol, 1,2-propanediol, 2,3-butanediol, 1,2-diisopropylethanediol, 5,6-decanediol, and 1,2-dicyclohexylethanediol;

R¹ is selected from the group:

ethyl, n-propyl, i-propyl, n-butyl, allyl, 2,2,2-trifluoroethyl, 2,2-difluoroethyl, 3,3,3-trifluoropropyl, 4,4,4-trifluorobutyl, and 3-butenyl;

R² is H;

R³ is selected from the group:

n-propyl, n-butyl, i-butyl, n-pentyl, neo-pentyl, cyclohexylmethyl,
cyclopentylmethyl, phenyl, benzyl, t-butoxymethyl, benzyloxymethyl,
hydroxymethyl, methoxymethyl, ethoxymethyl, propoxymethyl, and i-
propoxymethyl;

R⁴ is selected from the group:

methyl, ethyl, n-propyl, i-propyl, n-butyl, i-butyl, sec-butyl, t-butyl, phenyl,
benzyl, and phenethyl;

R⁵ is H or Q-R^{5a};

Q is 0, 1, or 2 amino acids;

R^{5a} is selected from the group:

-S(O)₂R⁶, -C(O)R⁶, -C(O)OR⁸, -C(O)NHR⁶, and -CH₂-R^{6a};

R⁶ is selected from the group:

methyl substituted with 0-3 R^c;
ethyl substituted with 0-3 R^c;
propyl substituted with 0-3 R^c;
butyl substituted with 0-3 R^c;
phenyl substituted with 0-3 R^c;
naphthyl substituted with 0-3 R^c;
benzyl substituted with 0-3 R^c; and
quinolinyl substituted with 0-3 R^c;

R^{6a} is selected from the group:

phenyl substituted with 0-3 R^c;
naphthyl substituted with 0-3 R^c;

benzyl substituted with 0-3 R^c; and
quinoliny substituted with 0-3 R^c;

R^c is selected at each occurrence from the group:

methyl, ethyl, n-propyl, i-propyl, n-butyl, i-butyl, t-butyl, methoxy, ethoxy,
propoxy, i-propoxy, CF₃, OCF₃, Cl, F, Br, I, OH, phenyl, C(O)OH, NH₂, -
CN, and NO₂;

R⁸ is methyl, ethyl, n-propyl, i-propyl, n-butyl, i-butyl, t-butyl, phenyl, and benzyl; and

n is 1 or 2.

5. (Original) The method of claim 4 wherein:

X is a boronic acid or a boron ester of formula BY¹Y²;

Y¹ and Y² are individually selected from C₁-C₆ alkoxy, or when taken together, Y¹ and
Y² form a cyclic boron ester where said chain or ring contains from 2 to 14
carbon atoms;

R¹ is selected from the group:

ethyl, n-propyl, i-propyl, n-butyl, i-butyl, allyl, 2,2,2-trifluoroethyl, 2,2-
difluoroethyl, 3,3,3-trifluoropropyl, 4,4,4-trifluorobutyl, and 3-butenyl;

R² is H;

R³ is selected from the group:

i-butyl, neo-pentyl, cyclohexylmethyl, t-butoxymethyl, benzyloxymethyl,
hydroxymethyl, benzyl and phenyl;

R⁴ is selected from the group:

ethyl, n-propyl, i-propyl, R-2-butyl, S-2-butyl, phenyl, benzyl, and phenethyl;

R⁵ is selected from the group:

H,
benzyl,
m-methylphenylsulfonyl,
m-trifluoromethylphenylsulfonyl,
p-i-propylphenylsulfonyl,
p-propylphenylsulfonyl,
p-t-butylphenylsulfonyl,
p-carboxylphenylsulfonyl,
4-(1,1')biphenylsulfonyl,
1-naphthylsulfonyl,
2-naphthylsulfonyl,
8-quinolinylsulfonyl,
pyrazin-2-ylcarbonyl,
n-butylsulfonyl,
N-phenylaminocarbonyl,
N-(p-n-butylphenyl)aminocarbonyl,
benzyloxycarbonyl,
methoxycarbonyl,
t-butyloxycarbonyl,
benzoyl,
methanesulfonyl,
phenylsulfonyl,
o-nitrophenylsulfonyl,
m-nitrophenylsulfonyl, and
m-aminophenylsulfonyl; and

n is 1 or 2.

6. (Original) The method according to claim 5 wherein:

X is a boronic acid or boron ester, wherein the ester is a diol selected from the group:

pinanediol, pinacol, 1,2-ethanediol, 1,3-propanediol, 1,2-propanediol, 2,3-butanediol, 1,2-diisopropylethanediol, 5,6-decanediol, and 1,2-dicyclohexylethanediol;

R¹ is selected from the group:

ethyl, n-propyl, i-propyl, n-butyl, i-butyl, allyl, 2,2,2-trifluoroethyl, 2,2-difluoroethyl, 3,3,3-trifluoropropyl, 4,4,4-trifluorobutyl, and 3-butenyl;

R² is H;

R³ is selected from the group:

i-butyl, neo-pentyl, cyclohexylmethyl, t-butoxymethyl, benzyloxymethyl, hydroxymethyl, benzyl, and phenyl;

R⁴ is selected from the group:

ethyl, n-propyl, i-propyl, R-2-butyl, S-2-butyl, phenyl, benzyl, and phenethyl;

R⁵ is selected from the group:

H,
benzyl,
m-methylphenylsulfonyl,
m-trifluoromethylphenylsulfonyl,
p-i-propylphenylsulfonyl,
p-propylphenylsulfonyl,
p-t-butylphenylsulfonyl,
p-carboxylphenylsulfonyl,
4-(1,1')biphenylsulfonyl,

1-naphthylsulfonyl,
 2-naphthylsulfonyl,
 8-quinolinylsulfonyl,
 pyrazin-2-ylcarbonyl,
 n-butylsulfonyl,
 N-phenylaminocarbonyl,
 N-(p-n-butylphenyl)aminocarbonyl,
 benzyloxycarbonyl,
 methoxycarbonyl,
 t-butyloxycarbonyl,
 benzoyl,
 methanesulfonyl,
 phenylsulfonyl,
 o-nitrophenylsulfonyl,
 m-nitrophenylsulfonyl, and
 m-aminophenylsulfonyl; and

n is 1 or 2.

7. (Original) The method according to claim 1 wherein said compound is selected from the group consisting of:

(1*R*)-1-((2*S*)-3-cyclohexyl-2-(3-isopropyl-3-((2*S*)-3-methyl-2-((2-pyrazinylcarbonyl)amino)butanoyl} amino)-2-oxo-1-pyrrolidiny)propanoyl} amino)-3-butenylboronic acid (+)-pinanediol ester;

(1*R*)-1-((2*S*)-3-cyclohexyl-2-(3-isopropyl-3-((2*S*)-3-methyl-2-((2-pyrazinylcarbonyl)amino)butanoyl} amino)-2-oxo-1-piperidiny)propanoyl} amino)-3-butenylboronic acid (+)-pinanediol ester;

(1R)-1-(((3-((methylsulfonyl)amino)-2-oxohexahydro-1*H*-azepin-1-yl)acetyl)amino)propylboronic acid (+)-pinanediol ester;

(1R)-1-(((2*S*)-2-(3-amino-3-isopropyl-2-oxo-1-pyrrolidinyl)-3-cyclohexylpropanoyl)amino)propylboronic acid (+)-pinanediol ester hydrochloride;

1R)-1-(((2*S*)-2-{3-(((1,1'-biphenyl)-4-ylsulfonyl)amino)-3-isopropyl-2-oxo-1-pyrrolidinyl}-3-cyclohexylpropanoyl)amino)propylboronic acid (+)-pinanediol ester;

(1R)-1-(((2*S*)-3-cyclohexyl-2-(3-isopropyl-2-oxo-3-(((4-propylphenyl)sulfonyl)amino)-1-pyrrolidinyl)propanoyl)amino)propylboronic acid (+)-pinanediol ester;

(1R)-1-(((2*S*)-3-cyclohexyl-2-{3-isopropyl-3-((1-naphthylsulfonyl)amino)-2-oxo-1-pyrrolidinyl}propanoyl)amino)propylboronic acid (+)-pinanediol ester;

(1R)-1-(((2*S*)-2-{3-((anilinocarbonyl)amino)-3-isopropyl-2-oxo-1-pyrrolidinyl}-3-cyclohexylpropanoyl)amino)propylboronic acid (+)-pinanediol ester;

(1R)-1-(((2*S*)-3-cyclohexyl-2-(3-isopropyl-3-(((3-methylphenyl)sulfonyl)amino)-2-oxo-1-pyrrolidinyl)propanoyl)amino)propylboronic acid (+)-pinanediol ester;

(1R)-1-(((2*S*)-3-cyclohexyl-2-(3-isopropyl-3-(((3-methylphenyl)sulfonyl)amino)-2-oxo-1-pyrrolidinyl)propanoyl)amino)propylboronic acid

(1R)-1-(((3-(((benzyloxy)carbonyl)amino)-3-isopropyl-2-oxo-1-pyrrolidinyl)(phenyl)acetyl)amino)propylboronic acid (+)-pinanediol ester;

(1*R*)-1-(((3-amino-3-isopropyl-2-oxo-1-pyrrolidinyl)(phenyl)acetyl)amino}propylboronic acid (+)-pinanediol ester hydrochloride;

(1*R*)-1-(((3-isopropyl-3-((methylsulfonyl)amino)-2-oxo-1-pyrrolidinyl}(phenyl)acetyl)amino}propylboronic acid (+)-pinanediol ester;

(1*R*)-1-(((3-isopropyl-2-oxo-3-(((4-propylphenyl)sulfonyl)amino)-1-pyrrolidinyl)(phenyl)acetyl)amino}propylboronic acid (+)-pinanediol ester;

(1*R*)-1-(((2*S*)-2-(3-(((benzyloxy)carbonyl)amino)-3-isopropyl-2-oxo-1-pyrrolidinyl)-4-methylpentanoyl)amino}propylboronic acid (+)-pinanediol ester;

(1*R*)-1-(((2*S*)-2-(3-amino-3-isopropyl-2-oxo-1-pyrrolidinyl)-4-methylpentanoyl)amino}propylboronic acid (+)-pinanediol ester hydrochloride;

(1*R*)-1-(((2*S*)-2-(3-isopropyl-3-((methylsulfonyl)amino)-2-oxo-1-pyrrolidinyl)-4-methylpentanoyl)amino)propylboronic acid (+)-pinanediol ester;

(1*R*)-1-(((2*S*)-2-(3-isopropyl-2-oxo-3-(((4-propylphenyl)sulfonyl)amino)-1-pyrrolidinyl)-4-methylpentanoyl)amino}propylboronic acid (+)-pinanediol ester;

(1*R*)-1-(((2*S*)-3-cyclohexyl-2-(3-ethyl-3-(((2*S*)-3-methyl-2-((2-pyrazinylcarbonyl)amino)butanoyl}amino)-2-oxo-1-pyrrolidinyl)propanoyl}amino)-3-butenylboronic acid (+)-pinanediol ester;

(1*R*)-1-(((2*S*)-2-(3-(((benzyloxy)carbonyl)amino)-3-isopropyl-2-oxo-1-piperidinyl)-3-cyclohexylpropanoyl)amino}propylboronic acid (+)-pinanediol ester;

(1*R*)-1-(((3-((tert-butoxycarbonyl)amino)-3-isopropyl-2-oxo-1-piperidinyl}(phenyl)acetyl)amino}propylboronic acid (+)-pinanediol ester;

(1*R*)-1-(((3-amino-3-isopropyl-2-oxo-1-piperidinyl)(phenyl)acetyl)amino}propylboronic acid hydrochloride (+)-pinanediol ester;

(1*R*)-1-(((3-isopropyl-3-((methoxycarbonyl)amino)-2-oxo-1-piperidinyl)(phenyl)acetyl)amino}propylboronic acid (+)-pinanediol ester;

(1*R*)-1-(((3-(benzoylamino)-3-isopropyl-2-oxo-1-piperidinyl)(phenyl)acetyl)amino}propylboronic acid (+)-pinanediol ester;

(1*R*)-1-(((3-isopropyl-3-((methylsulfonyl)amino)-2-oxo-1-piperidinyl)(phenyl)acetyl)amino}propylboronic acid (+)-pinanediol ester; and

(1*R*)-1-(((3-isopropyl-3-(((3-methylphenyl)sulfonyl)amino)-2-oxo-1-piperidinyl)(phenyl)acetyl)amino}propylboronic acid (+)-pinanediol ester;

(1*R*)-1-(((2*S*)-3-cyclohexyl-2-(3-isopropyl-3-(((2*S*)-3-methyl-2-((2-pyrazinylcarbonyl)amino)butanoyl}amino)-2-oxo-1-pyrrolidinyl)propanoyl}amino)-3-butenylboronic acid;

(1*R*)-1-(((2*S*)-3-cyclohexyl-2-(3-isopropyl-3-(((2*S*)-3-methyl-2-((2-pyrazinylcarbonyl)amino)butanoyl}amino)-2-oxo-1-piperidinyl)propanoyl}amino)-3-butenylboronic acid;

(1*R*)-1-(((3-((methylsulfonyl)amino)-2-oxohexahydro-1*H*-azepin-1-yl}acetyl)amino}propylboronic acid (+)-;

(1*R*)-1-(((2*S*)-2-(3-amino-3-isopropyl-2-oxo-1-pyrrolidinyl)-3-cyclohexylpropanoyl)amino}propylboronic acid;

1*R*)-1-(((2*S*)-2-{3-(((1,1'-biphenyl)-4-ylsulfonyl)amino)-3-isopropyl-2-oxo-1-pyrrolidinyl}-3-cyclohexylpropanoyl)amino}propylboronic acid;

(1R)-1-(((2*S*)-3-cyclohexyl-2-(3-isopropyl-2-oxo-3-(((4-propylphenyl)sulfonyl)amino)-1-pyrrolidinyl)propanoyl)amino)propylboronic acid;

(1R)-1-(((2*S*)-3-cyclohexyl-2-{3-isopropyl-3-((1-naphthylsulfonyl)amino)-2-oxo-1-pyrrolidinyl}propanoyl)amino)propylboronic acid;

(1R)-1-(((2*S*)-2-{3-((anilincarbonyl)amino)-3-isopropyl-2-oxo-1-pyrrolidinyl}-3-cyclohexylpropanoyl)amino)propylboronic acid;

(1R)-1-(((3-(((benzyloxy)carbonyl)amino)-3-isopropyl-2-oxo-1-pyrrolidinyl)(phenyl)acetyl)amino)propylboronic acid;

(1R)-1-(((3-amino-3-isopropyl-2-oxo-1-pyrrolidinyl)(phenyl)acetyl)amino)propylboronic acid (+)-hydrochloride;

(1R)-1-(((3-isopropyl-3-((methylsulfonyl)amino)-2-oxo-1-pyrrolidinyl)(phenyl)acetyl)amino)propylboronic acid;

(1R)-1-(((3-isopropyl-2-oxo-3-(((4-propylphenyl)sulfonyl)amino)-1-pyrrolidinyl)(phenyl)acetyl)amino)propylboronic acid;

(1R)-1-(((2*S*)-2-(3-(((benzyloxy)carbonyl)amino)-3-isopropyl-2-oxo-1-pyrrolidinyl)-4-methylpentanoyl)amino)propylboronic acid;

(1R)-1-(((2*S*)-2-(3-amino-3-isopropyl-2-oxo-1-pyrrolidinyl)-4-methylpentanoyl)amino)propylboronic acid hydrochloride;

(1R)-1-(((2*S*)-2-{3-isopropyl-3-((methylsulfonyl)amino)-2-oxo-1-pyrrolidinyl}-4-methylpentanoyl)amino)propylboronic acid;

(1*R*)-1-(((2*S*)-2-(3-isopropyl-2-oxo-3-(((4-propylphenyl)sulfonyl)amino)-1-pyrrolidinyl)-4-methylpentanoyl)amino}propylboronic acid;

(1*R*)-1-(((2*S*)-3-cyclohexyl-2-(3-ethyl-3-(((2*S*)-3-methyl-2-((2-pyrazinylcarbonyl)amino)butanoyl}amino)-2-oxo-1-pyrrolidinyl)propanoyl}amino)-3-butenylboronic acid;

(1*R*)-1-(((2*S*)-2-(3-(((benzyloxy)carbonyl)amino)-3-isopropyl-2-oxo-1-piperidinyl)-3-cyclohexylpropanoyl)amino}propylboronic acid;

(1*R*)-1-(((3-(((tert-butoxycarbonyl)amino)-3-isopropyl-2-oxo-1-piperidinyl)(phenyl)acetyl)amino}propylboronic acid;

(1*R*)-1-(((3-amino-3-isopropyl-2-oxo-1-piperidinyl)(phenyl)acetyl)amino}propylboronic acid hydrochloride;

(1*R*)-1-(((3-isopropyl-3-((methoxycarbonyl)amino)-2-oxo-1-piperidinyl)(phenyl)acetyl)amino}propylboronic acid;

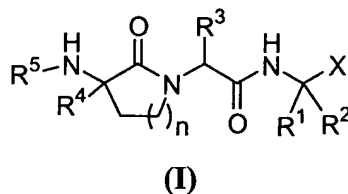
(1*R*)-1-(((3-(benzoylamino)-3-isopropyl-2-oxo-1-piperidinyl)(phenyl)acetyl)amino}propylboronic acid;

(1*R*)-1-(((3-isopropyl-3-((methylsulfonyl)amino)-2-oxo-1-piperidinyl)(phenyl)acetyl)amino}propylboronic acid; and

(1*R*)-1-(((3-isopropyl-3-(((3-methylphenyl)sulfonyl)amino)-2-oxo-1-piperidinyl)(phenyl)acetyl)amino}propylboronic acid;

or a pharmaceutically acceptable salt form thereof.

8. (Original) A method for inhibiting proteasome which comprises contacting a mammal in need thereof with a therapeutically effective amount of a compound of Formula I:



or a stereoisomer or pharmaceutically acceptable salt form thereof, wherein:

the lactam ring of Formula (I) is substituted with 0-2 R^b;

X is selected from the group:

B(OH)₂, BY¹Y², and C(=O)C(=O)NHR^{1a};

Y¹ and Y² are independently selected from:

- a) -OH,
- b) -F,
- c) -NR¹⁸R¹⁹,
- d) C₁-C₈ alkoxy, or

when taken together, Y¹ and Y² form:

- e) a cyclic boron ester comprising from 2 to 20 carbon atoms, and, optionally, 1, 2, or 3 heteroatoms which can be N, S, or O;
- f) a cyclic boron amide comprising from 2 to 20 carbon atoms and, optionally, 1, 2, or 3 heteroatoms which can be N, S, or O; or
- g) a cyclic boron amide-ester comprising from 2 to 20 carbon atoms and, optionally, 1, 2, or 3 heteroatoms which can be N, S, or O;

R¹ is selected from the group:

C₁₋₁₀ alkyl substituted with 0-3 R^a;

C₂₋₁₀ alkenyl substituted with 0-3 R^a;
C₂₋₁₀ alkynyl substituted with 0-3 R^a; and
C₃₋₆ cycloalkyl substituted with 0-3 R^a;

R^{1a} is selected from the group:

C₁₋₁₀ alkyl substituted with 0-3 R^a;
C₂₋₁₀ alkenyl substituted with 0-3 R^a;
C₂₋₁₀ alkynyl substituted with 0-3 R^a; and
C₃₋₆ cycloalkyl substituted with 0-3 R^a;

R^a is selected at each occurrence from the group:

C₁₋₃ alkyl, C₃₋₆ cycloalkyl, Cl, F, Br, I, CF₃, OH, =O, C₁₋₆ alkoxy, SH,
-S-C₁₋₆ alkyl;
phenyl substituted with 0-3 R^b;
naphthyl substituted with 0-3 R^b;
-O-(CH₂)_q-phenyl substituted with 0-3 R^b;
-O-(CH₂)_q-naphthyl substituted with 0-3 R^b; and
5-10 membered heteroaryl consisting of carbon atoms and 1-4 heteroatoms
selected from the group:
O, S, and N, and substituted with 0-3 R^b;

R^b is selected at each occurrence from the group:

C₁₋₆ alkyl, Cl, F, Br, I, OH, C₁₋₆ alkoxy, -CN, -NO₂, C(O)OR⁷, NR^dR^d, CF₃,
OCF₃, and C₃₋₆ cycloalkyl;

R² is H;

alternatively, R¹ and R² combine to form a C₃₋₅ cycloalkyl group;

R³ is selected from the group:

C₁₋₆ alkyl substituted with 0-2 R^a;
C₂₋₆ alkenyl substituted with 0-2 R^a;
C₂₋₆ alkynyl substituted with 0-2 R^a;
-(CH₂)_q-C₃₋₆ cycloalkyl substituted with 0-2 R^a;
-(CH₂)_q-phenyl substituted with 0-2 R^a;
-(CH₂)_q-naphthyl substituted with 0-2 R^a; and
-(CH₂)_q-5-10 membered heteroaryl consisting of carbon atoms and 1-4
heteroatoms selected from the group: O, S, and N, and substituted with 0-2
R^a;

R⁴ is selected from the group:

H;
C₁₋₆ alkyl substituted with 0-3 R^b;
phenyl substituted with 0-3 R^b;
benzyl substituted with 0-3 R^b; and
phenethyl substituted with 0-3 R^b;

R⁵ is H or Q-R^{5a};

Q is 0, 1, 2, or 3 amino acids;

R^{5a} is selected from the group:

-S(O)R⁶, -S(O)₂R⁶, -C(O)R⁶, -C(O)OR⁸, -C(O)NHR⁶, C₁₋₃ alkyl-R^{6a}, C₂₋₆
alkenyl-R^{6a}, and C₂₋₆ alkynyl-R^{6a};

R⁶ is selected from the group:

C₁₋₆ alkyl substituted with 0-3 R^c;
phenyl substituted with 0-3 R^c;

naphthyl substituted with 0-3 R^c;
benzyl substituted with 0-3 R^c; and
5-10 membered heteroaryl consisting of carbon atoms and 1-4 heteroatoms
selected from the group: O, S, and N, substituted with 0-3 R^c;

R^{6a} is selected from the group:

phenyl substituted with 0-3 R^c;
naphthyl substituted with 0-3 R^c;
benzyl substituted with 0-3 R^c; and
5-10 membered heteroaryl consisting of carbon atoms and 1-4 heteroatoms
selected from the group: O, S, and N, substituted with 0-3 R^c;

R^c is selected at each occurrence from the group:

C₁₋₄ alkyl, C₁₋₄ alkoxy, CF₃, OCF₃, Cl, F, Br, I, =O, OH, phenyl, C(O)OR⁷,
NR^dR^d, -CN, and NO₂;

R^d is selected at each occurrence from the group:

H and CH₃;

R⁷ is selected at each occurrence from the group:

H and C₁₋₆ alkyl;

R⁸ is selected from the group:

C₁₋₆ alkyl, benzyl, and C₃₋₆ cycloalkyl-methyl;

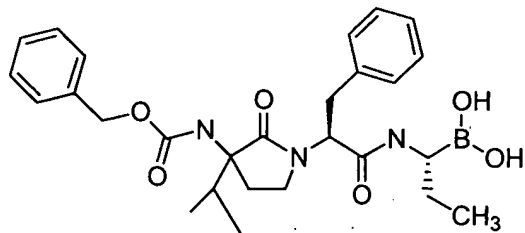
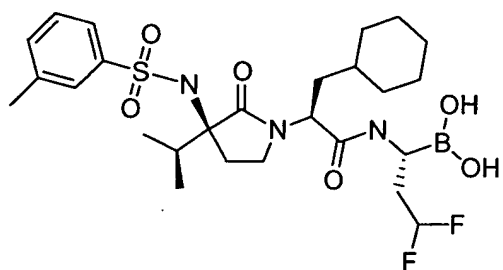
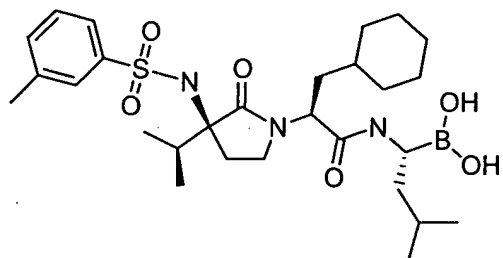
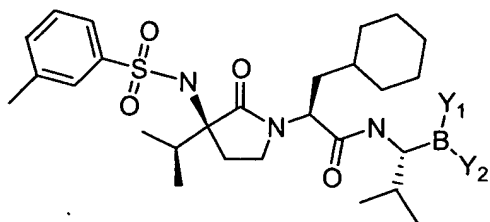
R¹⁸ and R¹⁹ at each occurrence are independently selected from H, C₁-C₄ alkyl, aryl(C₁-
C₄ alkyl)-, and C₃-C₇ cycloalkyl;

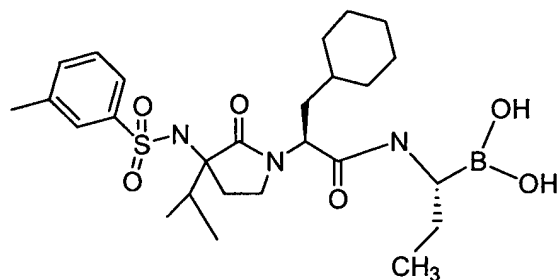
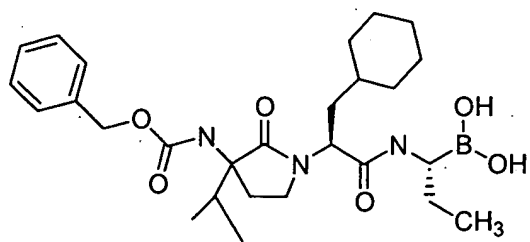
n is selected from the group:

1, 2, and 3; and

q is 0, 1, or 2.

9. (Original) The method of claim 8 wherein said compound is one of the following:





10. (Currently amended) A pharmaceutical composition comprising a therapeutically effective amount to reduce tumor growth rates, induce tumor regression or treat the symptoms of cancer of the compound of claim 1 and a pharmaceutically acceptable carrier.